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Allyson Reid

University of Connecticut - Storrs, twinkletoes1001@aol.com

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Running head: CORTISOL AND STRESS IN PATIENTS UNDERGOING
COLONOSCOPY

Salivary cortisol, psychological stress and depressive symptoms among patients
undergoing colon cancer screenings

Allyson Reid

Under the advisement of Dean Cruess, Ph.D.

Department of Psychology

University of Connecticut

Storrs, CT

Abstract

As the second leading cause of cancer-related deaths in the United States, colon cancer has a high cure rate if detected early by a colonoscopy (U.S. Cancer Statistics Working Group, 2007). However, more than 41 million at-risk Americans are not properly receiving colonoscopy screenings according to the recommendations of the Center for Disease Control. This study provides insight into the physiological and psychological benefits of the colonoscopy procedure over and above cancer detection and prevention. Thirty-six patients receiving colonoscopic screening at the University of Connecticut Health Center participated in this study. A questionnaire battery that assessed perceived stress, depressive symptoms, colon cancer related worry, and social support, and optional saliva sampling was completed 2 weeks prior to and post colonoscopy. It was hypothesized that salivary cortisol concentrations, perceived stress, and self-reported depressive symptoms would show significant decreases from pre to post colonoscopy, and that these variables would all be positively correlated with one another. Results showed significant, positive correlations between depressive symptoms and both salivary cortisol ($r(34) = .348, p < .05$) and perceived stress ($r(34) = .635, p < .01$). Morning salivary cortisol levels decreased significantly from pre to post colonoscopy to levels below the population mean ($t(16) = -3.711, p < .01$). No such differences were observed in either perceived stress or depressive symptoms. These results indicate that by decreasing cortisol concentrations to levels below that of the population mean, the colonoscopy provided physiological health benefits to patients beyond cancer screening. From a health psychology standpoint, this may encourage some of the 41 million Americans not receiving proper colon cancer screenings to adopt this potentially life-saving health behavior.

Salivary cortisol and psychological stress in patients undergoing colon cancer screenings

Maladaptive psychological factors have been shown to negatively impact physical health, affecting the morbidity and mortality rates across numerous medical conditions. Some of these include cardiovascular disease, hypertension, diabetes, asthma, irritable bowel syndrome, and migraines (Roy et al., 2001; Bradley, 1988; Mrazek & Klinnert, 1996). Chronic stress and depression tend to exacerbate physiological problems in healthy individuals, those at risk for developing disease, and current clinical populations seeking treatments. Central to this study, levels of stress and depressive symptomatology are also particularly related to cancer biomarkers, and may impact the morbidity and mortality of certain cancers, as well (Andersen et al., 1998; Bhagwagar et al., 2003). Much of the literature available in this area focuses primarily on patients already diagnosed with breast or prostate cancer, leaving room for inquiries regarding cancer prevention and screening. This study aims to investigate elements of both psychological and physical health within the context of an at-risk population undergoing colon cancer screenings.

Psychological Stress, Depression, and Cancer

Undoubtedly, the diagnosis and treatment of cancer is an inherently stressful experience for both patients and family members. The perception of psychological distress is common in individual case reports of cancer patients, and has been

observed in empirical studies as well (Sivesind & Baile, 2001). In rare cases, the patient's experience with cancer can precipitate the development of post-traumatic stress symptoms as a reaction to mounting stress (Cordova & Andrykowski, 2003). Accordingly, depressive symptoms are also commonly reported in patients suffering from nearly all forms of cancer (Massie, 2004). And while it is of interest to observe the effects of these maladaptive psychological functions in patients already diagnosed with cancers, the degree to which these variables contribute to diagnosis is also worth of exploration. In a study of women at-risk for developing breast cancer, those reporting greater levels of depressive symptoms and stress in daily life were found to have a 4-fold increased risk for developing breast cancer over those who did not share such a degree of mood alteration and daily stressful experiences (Kruk & Aboul-Enein, 2004).

While it is known that psychological factors such as stress and depression adversely affect the quality of life and daily functioning of cancer patients (Tsunoda et al., 2005), they have also been shown to negatively impact physiological processes leading to ill health. Reductions in immune system functioning were observed in breast cancer patients reporting higher levels of stress and depressive symptoms. Tumor surveillance mechanisms were disrupted, contributing to unchecked disease progression (Levy et al., 1987; Andersen et al, 1998). Another study linked psychological stress to increased colon cancer mortality rates (Kojima et al., 2005). In the realm of cancer detection, one study documented an association between psychological stress and physiological risk factors in patients receiving prostate cancer screenings. The men reporting higher degrees of psychological stress were

also found to have greater levels of prostate specific antigen, a marker present in large quantities in those with prostate cancer (Cohen et al, 2003; Stone et al, 1999). The same study also found that prostate cancer-specific worry was significantly associated with abnormal prostate antigen levels (Stone et al, 1999).

While cancer-specific worry may feed psychological stress, social support resources may buffer adverse affects. In a study conducted on cancer patients grouped by level of cancer-related worry, it was found that women and those with poor social support resources were more likely to have high levels of cancer-specific worry (Stefaneck et al., 1989). Social support networks have been associated with higher rates of elderly African-American women receiving mammography and occult stool examinations in the context of cancer prevention (Kang & Bloom, 1993). Thus, it appears that social support not only buffers stress when dealing with cancer diagnosis, but also contributes to better health behaviors by encouraging screening procedures.

Cortisol and Cancer

Cortisol is the primary glucocorticoid stress hormone secreted from the adrenal cortex. Part of the hypothalamic pituitary adrenal (HPA) axis, cortisol demonstrates a predictable diurnal pattern. Serum levels are highest approximately 30-60 minutes upon waking, and decrease over the course of the day, with the lowest serum concentration achieved after 3-5 hours into sleep (Stone et al., 2001). This normal diurnal pattern is driven by the amount of light transmitted through the retina to the hypothalamus (Weyerbrock et al., 1996). In stressful situations, however, cortisol levels elevate quickly to aid in returning the body to homeostasis.

Serum levels are highly correlated with salivary levels, as it represents unbound, and biologically available levels of cortisol (Kirschbaum & Hellhammer, 1994), and is much easier to access for research studies. Elevated salivary cortisol is found in patients experiencing depressive states and well as stressful conditions (Bhagwagar et al., 2003). Thus, it is a reliable bio-indicator of individuals' responses to stressful conditions and depression.

The disruption of proper cortisol levels is a well-documented phenomenon observed in breast cancer patients. Persistent elevations, erratic peaks and troughs, as well as stagnant concentrations have all been observed in cancer patient populations (Akbulut et al, 1999; Haus et al, 2001; Touitou et al., 1996; Pompe et al., 1996). It is likely that elevation and erratic patterns are the results of increased stress levels, depression and related states of distress (Vedhara et al., 2006; Dettenborn et al., 2005; Bower et al., 2005; Giese-Davis et al., 2004). Stagnant patterns, in which cortisol levels do not fluctuate throughout the day, may represent individuals experiencing a burnout of the HPA axis. Seen in individuals experiencing chronically high levels of stress, the HPA axis may become overworked and fail to function properly (Pruessner et al., 1999). Studies examining cortisol levels in patients with colon cancer demonstrated disruptions similar, though lesser in magnitude, to those observed in breast cancer patients (Mussi et al., 2003; Crippa et al, 2003; Mromon et al., 2002). Though important findings, these studies focused on patients with metastatic colon cancer, and may not properly represent the entire population of colon cancer patients. The only branch of inquiry into the relationship of psychological and physiological factors specifically related to colon cancer found

that music therapy during colonoscopy resulted in decreased salivary cortisol levels, presumably through reductions in stress (Uedo et al., 2004).

Disruption of cortisol concentration is not only problematic for responses to stressors, but may also affect cancer mortality rates. Metastatic breast cancer patients subjected to disruption of cortisol concentration for 3 consecutive days showed increased mortality rates up to 7 years after completion of the study (Sephton et al., 2000). Thus, disruption of the diurnal cortisol pattern was predictive of survival time in these patients. Although the disruptions of cortisol seen in cancer patients may affect morbidity and mortality rates, little is known of the potential mechanisms underlying this association. Perhaps heightened levels of stress and depression cause alterations in HPA axis functioning, as evidenced by abnormal cortisol levels. This may impair the functioning of the immune system, contributing to the development and progression of cancer (Spiegel & Giese-Davis, 2003).

Colon Cancer

To expand the breadth of knowledge in this field, this study focuses on individuals undergoing routine cancer screenings for colon cancer. As the second leading cause of cancer-related deaths in the United States, 53,000 individuals died from colon cancer in 2004 alone (U.S. Cancer Statistics Working Group, 2007). Men and women are equally susceptible, though men are slightly more likely to be diagnosed with colon cancer than women. Across racial and ethnic groups, African-Americans demonstrate increased incidence and mortality rates of colon cancer, as compared to Caucasians and Latinos (American Cancer Society, 2005). The primary

risk factor is advancing age, with approximately 90% of cases occurring in people aged 50 and over. Major physiological risk factors include inflammatory bowel disease, and a family history of colorectal cancer or polyps. Lifestyle choices, such as lack of regular physical activity, low fruit and vegetable intake, a low fiber-high fat diet, alcohol and tobacco consumption, and being overweight or obese also contribute to increased overall risk of developing colon cancer (National Institute of Health, Prevention, 2008). While some of these risk factors are inevitable, namely age and family history, many of the lifestyle choices are unfortunately common in today's society. Despite the fact that colon cancer is a significant health threat for many Americans, it is easily screened for and curable if caught at an early stage (National Institute of Health, Treatment, 2008).

Colonoscopy, the most widely used colon cancer screening procedure, involves the insertion of a fiber-optic camera through the anal opening to view the rectum and most distal portions of the large intestine (National Institute of Health, Prevention, 2008). If suspicious abnormal growths, known as polyps, are discovered in the patient's intestine, the physicians can surgically remove them at the time of the colonoscopy. Polyps removed and sent for biopsy may be completely benign, pre-cancerous growths, or actual colon cancer tumors. According to the American Academy of Family Physicians, in the case of pre-cancerous growths and stage 1 cancerous tumors, surgical removal is oftentimes sufficient to cure the condition. Despite the obvious necessity of colon cancer screenings, a colonoscopy is not the most comfortable of situations for patients, especially the preparation required prior to the procedure. The colon must be completely cleared for the physician to get an

accurate view of the intestinal wall, requiring the use of strong laxatives and prohibiting the ingestion of anything other than clear liquids in the 24-48 hours prior to the procedure (National Institute of Health, Treatment, 2008). This may be a factor deterring the 41.8 million Americans aged 50 and over not currently receiving adequate colonoscopic screenings according to the Center for Disease Control guidelines from adopting this potentially life-saving health behavior (U.S. Cancer Statistics Working Group, 2007).

Rationale and Hypotheses

To date, no study has examined the association between cortisol level and the psychological factors of stress and depression within the context of colon cancer prevention. The study aimed to answer the following question: Is the act of receiving a colonoscopy, irrespective of the outcome of the test, affecting psychological and other markers of physical health? Specifically, the variables of interest in this study were salivary cortisol levels, depressive symptoms, perceived stress, colon cancer-related worry, and social support. It was hypothesized that higher levels of both perceived stress and depressive symptoms would be positively correlated with salivary cortisol levels. This expectation is in accordance with the body of literature associating these variables. As an individual experiences either a stressful or depressive state, the HPA axis compensates by releasing more cortisol into the body system (Stone et al., 1999; Kirschbaum & Hellhammer, 1994). It was also hypothesized that salivary cortisol concentration, perceived stress, and depressive symptoms would all show significant decreases from pre- to post-colonoscopy. This result seems likely if the participants found the colonoscopy to be

a stressful event. In such a case, the resolution of this stressor should allow for decreases in both the psychological faculties and the stress biomarker.

No expectations were specifically made regarding colon cancer-related worry because of the novelty of the assessment scale used in this study. From previous research, it appears likely that cancer-related worry would be correlated with perceived stress, depressive symptoms and salivary cortisol levels, if the colonoscopy were viewed as a major stressor. However, the newness of the measure limits the basis from which to draw hypotheses. General findings and trends were investigated and discussed for possible implications. Social support was included as a mitigating factor to buffer those suffering from high levels of stress and depressive symptoms from the physiological manifestation of stress.

Method

Participants

Thirty-six patients scheduled to receive colonoscopic cancer screenings as part of the Colon Cancer Prevention Program at the University of Connecticut Health Center (UCHC) were recruited for participation in this study. For inclusion, participants were necessarily aged 50 and over with either a family history of colorectal cancer and/or heightened personal risk resulting from other known risk factors. At time 1, the sample consisted of 36 participants (19 females and 17 males). At time 2, the sample dropped a considerable number to a total of 12 participants (6 females and 6 males). The attrition rate was not due to any

experimental condition or characteristic of the particular population. During recruitment, there was a misunderstanding regarding the specific timeline of the study, leaving participants unaware of the follow-up scheduled for time 2. Though this decreased the number of returning participants, the problem was realized quickly and rectified. Following this, recruitment proceeded well, with many patients fully completing all portions of the study.

Materials

Psychometric Measures. The questionnaire battery consisted of 4 psychological measures designed to assess perceived stress, self-report depressive symptoms, colon cancer-related worry, and social support. The Perceived Stress Scale, PSS, (Cohen, Kamarck, & Mermelstein, 1983), a 14-item self-report Likert scale, was administered to measure the impact of daily stressors on personal functioning within the previous month. Higher scores on this scale indicated a higher perception of stress in daily life. This scale was of particular relevance to this study as it includes questions assessing the participant's perceived level of control over daily life stressors. The feeling of personal loss of control is an integral component of perception and manifestation of stress, especially within the realm of medical populations (Mineka & Kelly, 1989). Through the use of this measure, psychological stress was assessed. The Center for Epidemiologic Studies Depression Scale (CES-D) is a 20-item self-report scale that measures acute psychological distress and depressive symptomatology. Since this measure assesses depressive thoughts and feelings only over the previous week, it more accurately measures dysphoria, unpleasantness and discomfort in mood, and not major clinical

depression (Radloff, 1977). As with the PSS, higher scores on the CES-D indicate the presence of more depressive symptoms.

The Colon Cancer Worry scale is an unpublished measure created by Dean Cruess, Ph.D. at the University of Connecticut to assess the colon cancer-specific thoughts and worries regarding potential colorectal cancer diagnosis (Appendix). This measure was included as a means for obtaining insight into the enduring emotional and cognitive events surrounding fear of diagnosis. Using a 4-point Likert scale, positive scores on this measure indicate increasing amounts of active worrying and intrusive fear of colorectal cancer diagnosis. The final psychometric measure included in the questionnaire battery was the Interpersonal Support Evaluation List (Cohen & Hoberman, 1983), a 12-item self report measure assessing the participant's perception of the availability of social support resources across 3 major subtypes- appraisal, belonging, and tangible support. This measure was included in the battery to act as a moderator for those experiencing high levels of perceived stress, depressive symptoms and cancer-related worry. Those participants receiving high scores on this measure were considered to have ample social support to buffer the effects of challenges.

Salivary Sampling. To properly obtain and store participants' saliva samples, 143 2.0mL cryovials were purchased from Salimetrics, Inc., a leading laboratory supply company specializing in saliva collection and analysis. Two Extended Range High-Sensitivity Salivary Cortisol Enzyme Immunoassay Kits were also obtained from Salimetrics, Inc., allowing for the saliva samples to be assayed directly in the laboratory of Dr. Dan Rosenberg at UCHC where the samples were housed at -80°C.

Dr. Rosenberg's laboratory also provided the laboratory equipment necessary for the completion of this assay (Salimetrics, Inc., 2006).

Design and Procedure

This study was conducted at 2 time points scheduled approximately 1 month apart, with the colonoscopy procedure bisecting the study timeline equally, with time 1 and 2 occurring 2 weeks pre and post colonoscopy, respectively (Figure 1). At both time points, participants were instructed to complete the 10-minute questionnaire battery in their own homes. Additionally, optional saliva sampling was conducted on the morning of the same day to obtain cortisol concentrations and self-report data that displayed a high degree of temporal correspondence. Saliva collection was completed according to instructions given to the participants from Salimetrics, Inc (Salimetrics, Inc, 2006). Participants were asked to drool down the length of shortened plastic drinking straw into the cryovial until full. Certain restrictions were necessarily placed on the participants to ensure accurate cortisol levels in the saliva samples. Prior to collection participants were asked not to eat or drink for 1 hour, to abstain from alcohol consumption for 24 hours, and to avoid brushing their teeth for 2 hours, as these behaviors lead to alterations in baseline cortisol concentrations. Saliva sampling was conducted according to two optional timelines, either AM/PM sampling or morning rise. In the AM/PM method, a saliva sample was collected 1 hour upon awakening and 1 hour prior to bedtime. Though this schedule is easier for participants to complete, a more accurate measure of cortisol concentration is achieved using the morning rise timeline. For this method, 5 saliva samples were taken at 15 minute intervals over the first hour of awakening

at 0, 15, 30, 45, and 60 minutes. Regardless of the timeline of sampling, participants were instructed to freeze their samples in their home freezer and bring them in to their next appointment at UCHC.

Data Analysis

Psychometric Data. Questionnaire data was scored and entered into the computer for analysis by SPSS software. A correlation matrix was created comparing the total scores of the PSS, CES-D, Colon Cancer Worry scale, and the ISEL-12 both pre and post colonoscopy. Paired samples t-tests were also conducted on these totals to demonstrate whether significant changes occurred in these variables from pre- to post-colonoscopy.

Salivary Analysis. All 143 saliva samples were assayed for cortisol concentration at UCHC according to the protocol of the Salimetrics Extended Range High-Sensitivity Salivary Cortisol Enzyme Immunoassay Kit (Salimetrics, Inc.). The kits came preloaded with a standard amount of anti-cortisol monoclonal antibody in each well of the microtiter plate. When the samples were added, the cortisol present in the sample bound to the antibody, rendering the antibody unable to further complex with other available cortisol molecules. A standard, enzyme-linked cortisol was then added to bind the remaining available anti-cortisol antibodies. When the substrate for the enzyme was added to each well, a characteristic color change was produced. Measuring the amount of light transmitted through each individual well using a plate reader, the amount of enzyme-linked cortisol was determined. The inverse of this corresponded with the amount of cortisol present in each sample. Since participants were given the option of 2 salivary sampling

timelines, the data needed to be collapsed into one group before statistical analysis could proceed. Twenty-seven participants chose the AM/PM method, while only 7 conducted morning rise sampling. Since the AM sample was collected approximately 1 hour upon awakening, the 60 minute morning rise sample was determined to be the sample best temporally correspondent. In subsequent analyses, only the AM and 60 minute morning rise samples were included to increase the power of analysis.

The pre- and post-colonoscopy cortisol data was added to the correlation matrix to elucidate specific relational trends between the psychometric and physiological variables. Paired samples t-tests were conducted to determine if significant changes in salivary cortisol concentration were observed from pre- to post-colonoscopy. One sample t-tests were also conducted comparing the cortisol samples to the population mean of controls matched for age and gender to further describe any specifically observed change in cortisol concentration.

Results

Correlational Analysis

Pearsons' correlational analyses of perceived stress, depressive symptoms, colon cancer worry, social support and cortisol concentration yielded a couple of significant results across time points. Participants' scores on the PSS at time 1 and time 2 were significantly positively correlated ($r(10) = .631, p < .05$). A similar result was found for participants' scores on the CES-D from time 1 and time 2 ($r(10) = .696, p < .05$). For both of these variables, the more perceived stress or depressive symptoms experienced prior to the procedure, the higher were the scores

on those measures after the procedure. Neither Colon Cancer Worry ($r(10) = .200$, $p = .534$) nor the ISEL ($r(10) = .260$, $p = .414$) demonstrated significant correlations across time points. The correlation coefficient of AM cortisol concentration approached statistical significance across time points but did not achieve it outright given the small sample size ($r(17) = .415$, $p = .097$). PM cortisol concentration did not demonstrate a similar result ($r(9) = .417$, $p = .201$).

The subscales of the Colon Cancer Worry measure, Worry and Thoughts, were significantly positively correlated ($r(34) = .405$, $p < .05$) prior to the colonoscopy. This indicates that those participants experiencing worry regarding cancer diagnosis were also more likely to have intrusive thoughts as well. This finding was not replicated post-colonoscopy ($r(10) = .386$, $p = .215$). Post-colonoscopy, Colon Cancer Thoughts and perceived stress were significantly positively correlated ($r(10) = .611$, $p < .05$). Those experiencing more perceived stress after the procedure were also more likely to report greater levels of intrusive colon cancer-related thoughts. Interestingly, a special relationship was demonstrated between gender and colon cancer worry pre-colonoscopy. Women were found to have more colon cancer-related worries than men ($r(34) = .389$, $p < .05$).

Major correlational findings were discovered when examining the relationships of depressive symptoms, perceived stress, and AM cortisol concentrations prior to the colonoscopy. It was found that perceived stress and depressive symptoms were positively correlated with high significance ($r(34) = .635$, $p < .01$). Those participants indicating more depressive symptomatology also reported higher levels of perceived stress in their daily lives. The CES-D scores were

also significantly correlated with AM cortisol concentration ($r(34) = .348, p < .05$). The more depressive symptoms reported at time 1, the higher levels of the stress hormone cortisol were found in the saliva. See Figure 2 for the raw data distributions of the major output variables across time points.

T-test analysis and Cohen's d

Paired samples t-tests were conducted for the total scores on the 4 psychometric measures and both AM and PM cortisol concentrations across time points. Participants' scores on the CES-D, PSS, ISEL-12, or Colon Cancer Worry did not display any significant changes in value from pre- to post-colonoscopy. AM cortisol concentrations showed a highly significant decrease from time 1 to time 2 ($t(16) = -6.443, p < .01$). The Cohen's d calculated for this effect was -3.327 , indicating only a 5% overlap of mean cortisol concentrations across time points. A significant result was not found for the PM saliva samples ($t(10) = -1.062, p = .313$). See Figure 3 for a graphical representation of these relationships.

One sample t-tests were conducted separately for pre- and post-colonoscopy AM cortisol data to further elucidate the change in cortisol concentration with reference to population means for age and gender-matched controls. For men and women between the ages of 51 and 70, Salimetrics, Inc., reports an AM population mean of 0.58mg/dl. AM cortisol concentration pre-colonoscopy was found to be highly significantly increased above the population mean ($t(35) = 3.937, p < .01$). The Cohen's d calculated for the pre-colonoscopy data was given as $d = 1.37$, indicating a large positive effect. AM cortisol concentration post-colonoscopy was highly significantly decreased below the population mean ($t(16) = -3.711, p < .01$). The

Cohen's d calculated for the post-colonoscopy effect was found to be $d = -1.916$, indicating a large negative effect.

Discussion

While full support of the many-armed hypothesis was not achieved, the results of this study do solidly support many of the important claims made. The psychometric measures of perceived stress and depressive symptomatology did not significantly change after the colonoscopy procedure as hypothesized. However, the AM cortisol values decreased significantly from pre- to post-procedure. While it has been shown (Roy et al., 2001; Bradley, 1988; Mrazek & Klinnert, 1996) that psychological stressors are often simultaneously manifested physiologically, these results seem to indicate that psychological stressor can elude the realm of perception while demonstrating its effects in the body. Thus, it appears that though psychological stressors may cause changes in physiology, the element of awareness is not necessary. Self-report measures highlight this possibility, as an individual must perceive a modicum of psychological disruption before he is able to report it on a questionnaire. The results of this study seem to indicate that the colonoscopy appointment is a stressor that was not brought into awareness for cognitive processing. This is supported by the fact that an overwhelming majority of participants, 91.4%, indicated that they did not fear being diagnosed with colorectal cancer. Despite claiming to be unafraid of the possibility of diagnosis, the morning cortisol levels were significantly increased above the population mean.

One may put forth the argument that the participants showed increases in cortisol concentration not because they feared diagnosis, but rather because the

colonoscopy procedure itself acted as a stressor. This argument led to the inclusion of the one sample t-tests to further elucidate the exact nature of the changes occurring in morning cortisol concentration from pre- to post-colonoscopy. If the colonoscopy acted merely as an acute stressor, the post-colonoscopy cortisol data would show a high degree of correspondence with that of the general population. However, when comparing the sample data to the general population, it was found that not only did the morning cortisol concentration decrease from pre- to post-colonoscopy, but that it decreased to levels significantly below that of the population mean. This finding shows that the change in morning cortisol concentration was not just due to a resolution of a stressful event.

Further supporting this finding, Oswald et al (2004) demonstrated that cortisol levels elevated experimentally by an induced stressor tended to decrease back down to basal levels within one hour of resolution of the stressful event. One may argue that while a colonoscopy is indeed a stressful event in the lives of patients, it is not an acute stressor. Therefore, its effect on elevating cortisol concentrations may be prolonged past the 1-hour mark. The specific procedure conducted during a colonoscopy yields immediate results if no polyps are found in the patient's colon. In such an instance, the patient is notified upon waking from anesthesia that the colon was clear of suspicious growths. Presumably, those patients would not show a prolonged stress response since the event had a clearly defined, benign ending. Even in patients who have polyps removed for biopsy, the results of such tests usually take a week to learn from the pathology lab. At the 2-week time point post-colonoscopy, the patients should have all been well aware of

the outcome of their screenings. It is understandable that those patients receiving colon cancer diagnosis would show a prolonged stress response in dealing with that information, but without access to medical records the final outcome measures of the individual screens cannot be commented upon.

Correlational analyses, while insufficient to claim causality, offered some insight into specific relational trends of the main output variables of this study. The fact that both depressive symptomatology and perceived stress were positively correlated with themselves across time points, further supports the idea that not all stressors are accessible for cognitive processing and self-report, despite the physiological changes that may occur with stress hormone levels. It may be that the lack of availability to cognitively process the stress of the colonoscopy that leads to increased cortisol levels prior to the actual procedure. Anticipatory stress most likely contributed to the elevated cortisol concentrations, but was unfortunately not assessed using the PSS given the particular retrospective timeline used in the measure. The CES-D may hit on this anticipatory stress despite its retrospective focus, especially in the manifestations of stressful symptoms in changes in behavior, mood, and outlook, and issues of control. Perhaps this is the reason why correlations were seen with depressive symptoms and cortisol levels, but not with perceived stress as assessed by the PSS. Since the PSS and CES-D were positively correlated, it is evident that psychological stress is strongly related to negative changes in affect. It stands to reason that while the participants may have been unaware of the entirety of their psychological stress, as evidenced by the cortisol

data, they did notice changes in mood that represented the true magnitude of their stress.

Finally, only one major psychometric output demonstrated any specific relationship with gender. Women, who made up approximately 50% of the sample at either time point, reported a significantly greater amount of colon cancer-related worry than men. This phenomenon may be due to increased perceptions of concern for familial ties that may be negatively affected by a potential cancer diagnosis. Women tend to put the feelings and needs of others and ahead of their own, which may lead to more intrusive thoughts and worries about the possibility of colon cancer diagnosis. Also, women are more likely than men to use introspection to examine their thoughts, and more emotionally expressive in stressful situations (Fernandez-Ballesteros et al., 1998). This may feed the correlation of women seemingly experiencing more cancer-related worry than men. While this may be true, it also may be that women are just more adept at pinpointing the source of their stress and expressing it to others.

Implications

The colonoscopy not only provided the health benefits associated with cancer screening but also led to a decrease in cortisol concentration below that of the population mean. This is an important finding, since short term high cortisol has been implicated in abdominal weight gain, elevated blood glucose leading to insulin resistance, high blood pressure, osteoporosis, easy bruising, and disorders of the immune system (Roberts et al., 2007; Kertzner et al., 1993). Chronically, elevated cortisol is very dangerous to physical health. It can cause hormonal imbalances,

short-term memory loss, and contribute to Alzheimer's disease and senile dementia (Peavy et al., 2007). And while low cortisol levels are also maladaptive, the decrease from population mean observed in this sample would not qualify as pathologically low cortisol. In this sample, the lowered cortisol levels allow for quicker recovery from stress and decrease the potential risk factors of other health problems. This may encourage some of the 41.8 million Americans not following the proper screening timeline advocated by the Center for Disease Control to receive a colonoscopy once every decade. This study may educate the general public about the benefits of a colonoscopy, and contribute to greater awareness of colon cancer and its risk factors. From a health psychology standpoint, the findings of this study could encourage people to adopt potentially life-saving health behaviors, and contribute to the overall health and wellness of the population.

References

- Akbulut, H., Icli, F., Buyukcelik, A., Akbulut, K. G., & Demirci, S. (1999). The role of granulocyte-macrophage-colony stimulating factor, cortisol, and melatonin in the regulation of the circadian rhythms of peripheral blood cells in healthy volunteers and patients with breast cancer. *J Pineal Res*, *26*, 1-8.
- American Cancer Society. *Colorectal Cancer Facts and Figures Special Edition 2005*. Atlanta: American Cancer Society.
- Andersen, B. L., Farrar, W. B., Golden-Kreutz, D., et al. (1998). Stress and immune response after surgical treatment for regional breast cancer. *J Nat Cancer Inst*, *90*, 30-36.
- Bhagwagar, Z., Hafizi, S., & Cowen, P. J. (2003). Increase in concentration of waking salivary cortisol in recovered patients with depression. *Am J Psychiatry*, *160*, 1890-1891.
- Bower, J. E., Ganz, P. A., & Aziz, N. (2005). Altered cortisol response to psychologic stress in breast cancer survivors with persistent fatigue. *Psychosom Med*, *67*, 277-280.
- Bradley, C. (1988). Stress and diabetes. Handbook of life stress, cognition and health. 383-401. Oxford England: John Wiley & Sons.
- Cohen, L., Fouladi, R. T., Babaian, R.J., et al. (2003). Cancer worry is associated with abnormal prostate-specific antigen levels in men participating in a

- community screening program. *Cancer Epidemiology, Biomarkers & Prevention*, 12, 610-617.
- Cohen, S., & Hoberman, H. A. (1983). Positive events and social support as buffers of life change stress. *J App Soc Psych*, 13(2), 99-125.
- Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *J Health & Soc Behav*, 24(4), 385-396.
- Cordova, M. J., & Andrykowski, M. A. (2003). Responses to cancer diagnosis and treatment: posttraumatic stress and posttraumatic growth. *Semin Clin Neurophysiatry*, 8, 286-296.
- Crippa, S., Mussi, C., Angelini, C., Caprotti, R., Bonardi, C., Muselli, P., et al. (2003). Alteration of hypothalamus-pituitary-adrenal gland axis in colorectal cancer patients. Preliminary report. *Minerva Chir*, 58, 581-585.
- Dettenborn, L., James, G. D., van Berge-Landry, H., Vladimarsdottir, H. B., Montgomery G. H., & Bovbjerg, D. H. (2005). Heightened cortisol responses to daily stress in working women at familial risk for breast cancer. *Biol Psychol*, 69, 167-179.
- Fernandez-Ballesteros, R., Ruiz, M., & Garde, S. (1998). Emotional expression in healthy women and those with breast cancer. *Brit J Health Psych*, 3(1), 41-50.
- Giese-Davis, J., Sephton, S. E., Abercrombie, H. C., Duran, R. E., & Spiegel, D. (2004). Repression and high anxiety are associated with aberrant diurnal cortisol rhythms in women with metastatic breast cancer. *Health Psychol*, 23, 645-650.
- Haus, E., Dumitriu, L., Nicolau, G. Y., Bologa, S., & Sackett-Lundeen, L. (2001). Circadian rhythms of basic fibroblast growth factor (bFGF), epidermal growth factor (EGF), insulin-like growth factor-1 (IGF-1), insulin-like growth factor binding protein-3 (IGFBP-3), cortisol, and melatonin in women with breast cancer. *Chronobiol Int*, 18, 709-727.
- Kang, S. H., & Bloom, J.R. (1993). Social support and cancer screening among older black Americans. *J Natl Cancer Inst*, 85(9), 737-742.
- Kertzner, R., Goetz, R., Todak, G., & Cooper, T. (1993). Cortisol levels, immune status, and mood in homosexual men with and without HIV infection. *Am J Psychiatry*, 150(11), 1674-1678.
- Kirschbaum, C., & Hellhammer, D. H. (1994). Salivary cortisol in psychoneuroendocrine research: recent developments and applications. *Psychoneuroendocrinology*, 19, 313-333.

- Kojima, M., Wakai, K., Tokudome, S., Tamakoshi, K., Toyoshima, H., Watanabe, Y., et al. (2005). Perceived psychologic stress and colorectal cancer mortality: findings from the Japan Collaborative Cohort Study. *Psychosom Med*, 67, 72-77.
- Kruk, J. & Aboul-Enein, H. Y. (2004). Psychological stress and the risk of breast cancer: a case-control study. *Cancer Detect Prev*, 28, 399-408.
- Levy, S., Herberman, R., Kippman, M., et al. (1987). Correlation of stress factors with sustained depression of natural killer cell activity and prediction prognosis in patients with breast cancer. *J Clin Oncol*, 5, 348-353.
- National Institutes of Health. *Colorectal Cancer (PDQ): Treatment*. <http://www.cancer.gov/cancertopics/pdq/treatment/colon/patient>. Updated 4/28/08. Accessed 11/23/08.
- National Institutes of Health. *Colorectal Cancer (PDQ): Prevention*. <http://www.cancer.gov/cancertopics/pdq/prevention/colorectal/HealthProfessional/page3>. Updated 5/09/08. Accessed 11/23/08.
- Massie, M.J. (2004). Prevalence of depression in patients with cancer. *J Natl Cancer Inst Monogr*, 32, 57-71.
- Mineka, S., & Kelly, K. (1989). The relationship between anxiety, lack of control and loss of control. Stress, personal control and health (pp. 163-191). Oxford England: John Wiley & Sons.
- Mormon, M. C., Bogdan, A., Cormont, S., Touitou, Y., & Levi, F. (2002). Cortisol diurnal variation in blood and saliva of patients with metastatic colorectal cancer: relevance for clinical outcome. *Anticancer Res*, 22, 1243-1249.
- Mrazek, D., & Klinnert, M. (1996). *Emotional stressors and the onset of asthma. Severe stress and mental disturbance in children*. 211-224. Washington, DC US: American Psychiatric Association.
- Mussi, C., Angelini, C., Crippa, S., Caprotti, R., Fumagalli, L., Motta V., et al. (2003). Alteration of hypothalamus-pituitary-adrenal glands axis in colorectal cancer patients. *Hepatogastroenterology*, 50(Suppl 2), ccsviii-ccxxxi.
- Oswald, L., Mathena, J., & Wand, G. (2004). Comparison of HPA axis hormonal responses to naloxone vs psychologically-induced stress. *Psychoneuroendocrinology*, 29(3), 371-388.

- Peavy, G., Lange, K., Salmon, D., Patterson, T., Goldman, S., Gamst, A., et al. (2007). The effects of prolonged stress and APOE genotype on memory and cortisol in older adults. *Biological Psychiatry*, *62*(5), 472-478.
- Pompe, G. von der, Antoni, M. H., & Heijnen, C. J. (1996). Elevated basal cortisol levels and attenuated ACTH and cortisol responses to a behavioral challenge in women with metastatic breast cancer. *Psychoneuroendocrinology*, *21*, 361-374.
- Pruessner, J. C., Hellhammer, D. H., & Kirschbaum, C. (1999). Burnout, perceived stress and cortisol responses to awakening. *Psychosom Med*, *61*, 197-204.
- Radloff, L.S. (1977). The CES-D scale: A self report depression scale for research in the general population. *App Psych Measurement*, *1*, 385-401.
- Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L., et al. (2005). *SEER Cancer Statistics Review, 1975–2002*, National Cancer Institute. Bethesda, MD, based on November 2004 SEER data submission.
- Roberts, C., Troop, N., Connan, F., Treasure, J., & Campbell, I. (2007). The effects of stress on body weight: Biological and psychological predictors of change in BMI. *Obesity*, *15*(12), 3045-3055.
- Roy, M. P, Kirschbaum, C., Steptoe, A. (2001). Psychological, cardiovascular, and metabolic correlates of individual differences in cortisol stress recovery in young men. *Psychoneuroendocrinology*, *26*, 375-391.
- Salimetrics, Inc. *High Sensitivity salivary Cortisol Enzyme Immunoassay Kit 2006*; Catalog No. 1-0102/1-0112 96-Wel Kit, Updated: 6/23/04.
- Sephton, S. E., Sapolsky, R. M., Kraemer, H. C., & Spiegel, D. (2000). Diurnal cortisol rhythm as a predictor of breast cancer survival. *J Natl Cancer Inst*, *92*, 994-1000.
- Sivesind D., & Baile, W. F. (2001). The psychologic distress in patients with cancer. *Nurs Clin North Am*, *36*, 809-825.
- Speigel, D., & Giese-Davis, J. (2003). Depression and cancer: mechanisms and disease progression. *Biol Psychiatry*, *54*, 269-282.
- Stefanek, M. E., Shaw, A., DeGeorge, D., & Tsottles, N. (1989). Illness-related worry among cancer patients: prevalence, severity, and content. *Cancer Invest*, *7*(4), 365-371.

- Stone, A. A., Mezzacappa E. S., Donatone, B. A., et al. (1999). Psychological stress and social support are associated with prostate-specific antigen levels in men: Results from a community screening program. *Health Psychol*, *18*, 482-486.
- Swan J, Breen N, Coates RJ, Rimer BK, Lee NC. (2003). Progress in cancer screening practices in the United States: results from the National Health Interview Survey. *Cancer*, *97*(6), 1528-1540.
- Touitou, Y., Bogdan, A., Levi, F., Benavides, M., & Auzéby, A. (1996). Disruption of the circadian patterns of serum cortisol in breast and ovarian cancer patients; relationship with tumour marker antigens. *Br J Cancer*, *74*, 1248-1252.
- Tsunoda, A., Nakao, K., Hiratsuka, K., Yasuda, N., Shibusawa, M., & Kusano, M. (2005). Anxiety, depression and quality of life in colorectal cancer patients. *Int J Clin Oncol*, *10*, 411-417.
- Uedo, N., Ishikawa, H., Morimoto, K., Ishihara, R., Narahara, H., Akedo, I., et al. (2004). Reduction in salivary cortisol level by music therapy during colonoscopic examination. *Hepatogastroenterology*, *51*, 451-453.
- U.S. Cancer Statistics Working Group (2007). *United States Cancer Statistics: 2004 Incidence and Mortality*. Atlanta (GA): Department of Health and Human Services, Centers for Disease Control and Prevention, and National Cancer Institute.
- Vedhara, K., Stra, J. T., Miles, J. N., Sanderman, R., & Ranchor, A. V. (2006). Psychosocial factors associated with indices of cortisol production in women with breast cancer and controls. *Psychoneuroendocrinology*, *3*, 299-311.
- Weyerbrock, A., Timmer, J., Hohagen, F., & Berger, M. (1996). Effects of light and chronotherapy on human circadian rhythms in delayed sleep phase syndrome: Cytokines, cortisol, growth hormone, and the sleep-wake cycle. *Biol Psychiatry*, *40*(8), 794-797.

Appendix

Colon Cancer Worry Scale- unpublished measure created by Dean Cruess, Ph. D. at the University of Connecticut to assess colon cancer-specific patterns of thoughts and worries.

- 1 = Not at all or rarely
- 2 = Sometimes
- 3 = Often
- 4 = A lot

_____ During the past month, how often have you thought about your own chances of getting colorectal cancer?

_____ During the past month, how often have your thoughts about getting colorectal cancer affected your mood?

_____ During the past month, how often have your thoughts about getting colorectal cancer affected your ability to perform your daily activities?

_____ During the past month, how often have you worried about getting colorectal cancer?

1 = Strongly disagree

2 = Disagree

3 = Agree

4 = Strongly Agree

_____ I worry that I already have colorectal cancer.

_____ I fear being diagnosed with colorectal cancer.

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Figure Captions

Figure 1. Participants were instructed to complete the 10-minute questionnaire 2 weeks before and after their scheduled colonoscopy appointment. Optional saliva sampling was also conducted at each time point using either AM/PM or morning rise sample schedules.

Figure 2. Scatter plots of pre- and post-colonoscopy data were created to demonstrate correlations within variables across time points. Both depressive symptoms (CES-D) and perceived stress (PSS) were positively correlated with one another. AM cortisol concentration was not significantly correlated across time points. Note the similarity in the shape of the distributions of the CES-D and AM cortisol concentration. This indicates that the CES-D may have been a better indicator of stress levels than the PSS.

Figure 3. T-test analyses conducted on the mean cortisol concentrations across time points yielded significant results only for the morning samples. AM cortisol concentration was found to be highly significantly decreased from pre- to post-colonoscopy ($t(16) = -6.443, p < .01$). Double asterisks (**) indicate highly significant differences.

Figure 1. Timeline of experimental procedure followed by participants

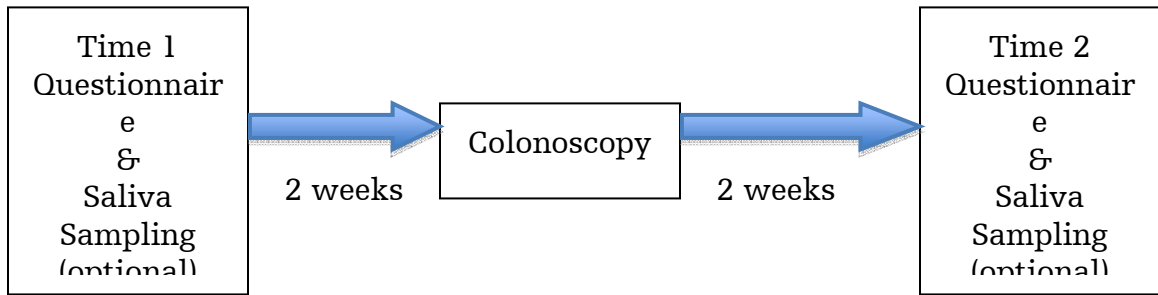


Figure 2. Raw data distributions of depressive symptoms, perceived stress, and cortisol concentration across time points

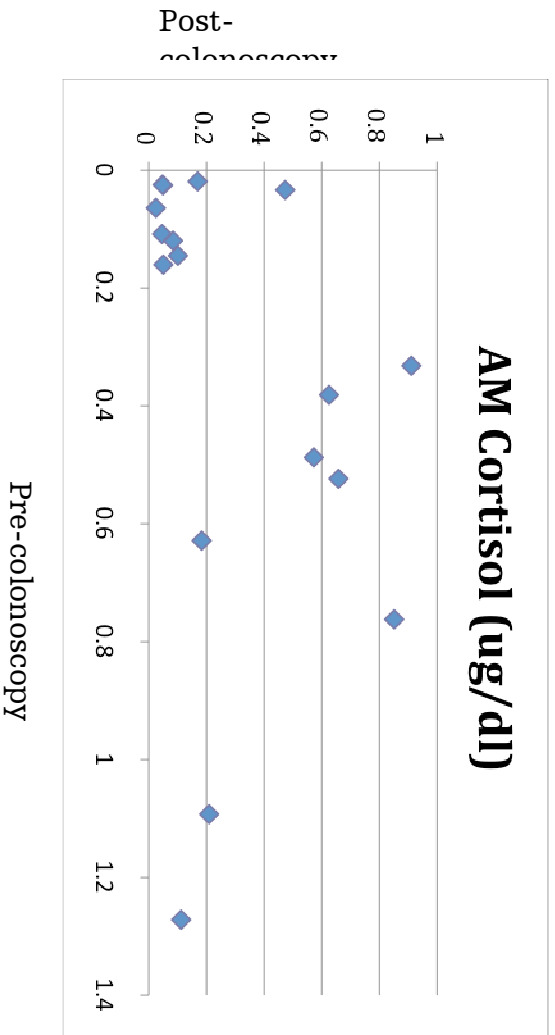
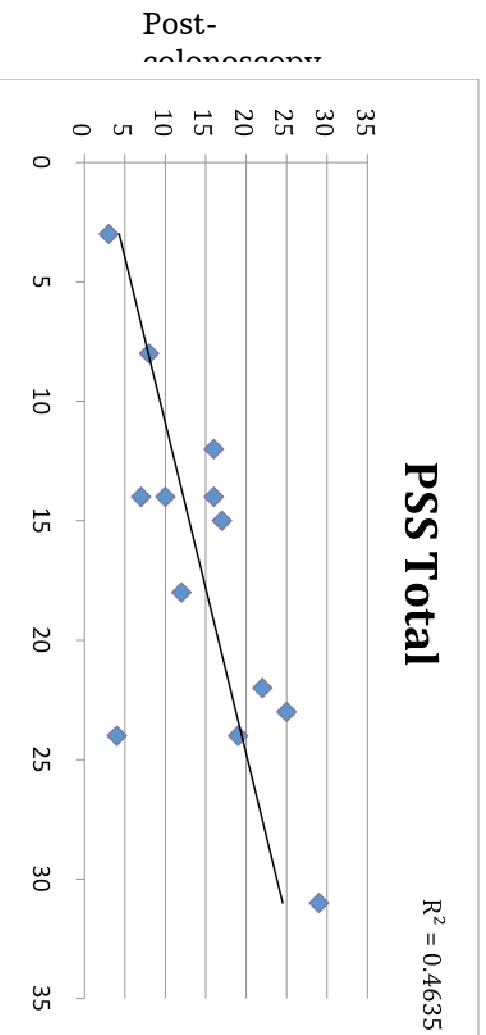
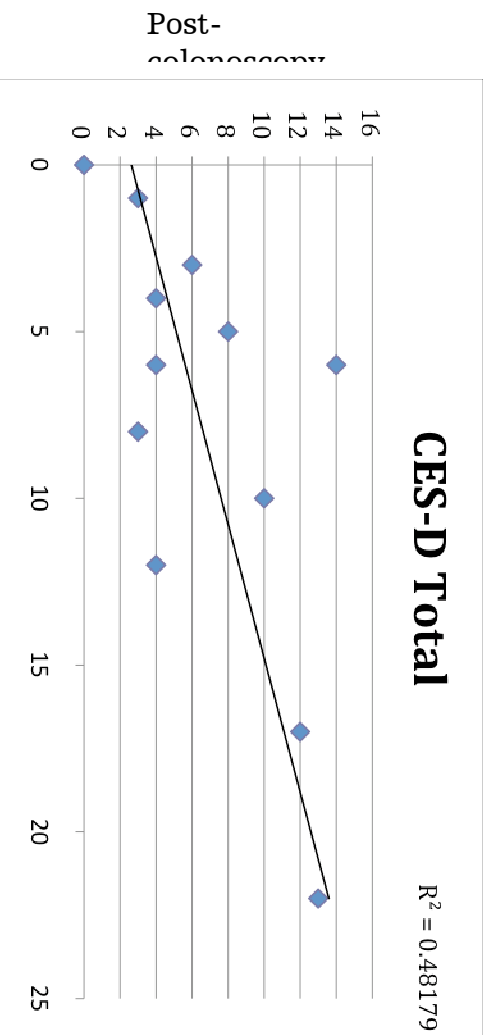


Figure 3. Comparison of mean AM and PM cortisol concentrations across time points

